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Bovine Campylobacteriosis: A Review

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SUMMARY

Campylobacteriosis (vibriosis) is a venereal disease of cattle caused by the organism *Campylobacter fetus* subspecies *fetus* previously known as *Vibrio fetus* subspecies *venerealis*. Characteristically the disease causes infertility in the female with an increased number of services necessary for conception. Abortions late in gestation are also occasionally seen. Most cases or outbreaks occur after the recent introduction of an infected bull or cow into a susceptible breeding herd. Often the disease remains undetected until late fall when the livestock owner recognizes that he has a number of females exhibiting estrus. A tentative diagnosis can be made by a study of the herd history and can often be confirmed by laboratory means.

In recent years many advances have been made towards establishing an understanding of the immune response that occurs with infection and systemic immunization. In this review, recommendations are made regarding the appropriate time to immunize the breeding herd against campylobacteriosis.

RÉSUMÉ

Une revue de la campylobactériose bovine

La campylobactériose, ou vibriose, est une maladie vénérienne des bovins, imputable à *Campylobacter fetus*, sous-espèce *fetus*; on connaissait auparavant ce micro-organisme, sous le nom de *Vibrio fetus*, sous-espèce *fetus*. La maladie provoque invariablement de l'infertilité chez la femelle qui requiert ultérieurement plusieurs saillies avant de concevoir. Des avortements surviennent aussi dans le dernier tiers de la gestation. La plupart des cas ou des éclosions de la maladie se produisent peu de temps après l'introduction d'un taureau ou d'une vache infectés dans un troupeau de reproduction susceptible. La maladie évolue souvent de façon silencieuse, jusqu'à la fin de l'automne, alors que le fermier constate que plusieurs de ses vaches manifestent un oestrus. Une histoire du troupeau permet de poser un diagnostic présomptif que des épreuves de laboratoire viennent souvent confirmer.

On a récemment réalisé beaucoup de progrès dans la compréhension de la réponse immunitaire qui résulte d'une infection spontanée ou d'une immunisation systémique. Dans le présent article, l'auteur fait des recommandations relatives au temps propice à l'immunisation des sujets d'un troupeau reproducteur contre la campylobactériose.

INTRODUCTION

Campylobacteriosis (vibriosis) is a venereal disease of cattle caused by the organism *Campylobacter fetus* subspecies *fetus*. In 1919 in a study of infectious abortion in cattle, a spirillium from aborted fetal fluids was isolated and named *Vibrio fetus*. Prior to 1973 this organism was identified by the name *Vibrio fetus* subspecies *venerealis*. In 1973 it was reclassified as *Campylobacter fetus* subspecies *fetus*. The change in nomenclature was the result of a study of the DNA content that indicated *Vibrio fetus* and *Vibrio bubulus* should be removed from the genus Vibrio, and a new genus, Campylobacter was proposed (19).

Bovine genital campylobacteriosis results primarily in transient infertility of female cattle associated with inflammation of the reproductive tract, while infection of the male results in an asymptomatic carrier state (16).

In western Canada and the United States this disease has been an important cause of infertility in beef cattle (12). With the advent and widespread usage of vaccines, the incidence has dropped dramatically but the disease still occurs sporadically, causing large economic losses.

ETIOLOGY

The causative organism has been named *Campylobacter fetus* subspecies *fetus* (19). Members of the genus Campylobacter are small Gram-negative, microaerophilic, curved to spiral rods that have a single polar flagellum. They are motile with a characteristic corkscrew kind of movement.

Closely related subspecies of *C. fetus* are *C. fetus* subspecies *intestinalis* and *C. fetus* subspecies *jejuni*. Neither of these two subspecies are involved with the venereal disease of cattle although *C. fetus* subspecies *intestinalis* occasionally causes abortion in cattle (2). *Campylobacter sputorum* subspecies *bubulus* was previously called *Vibrio bubulus* (19) and is a nonpathogenic inhabitant of the genital tract of sheep and cattle.

CLINICAL FEATURES

Campylobacteriosis is characterized by infertility with an increased number

of services necessary for conception. Early embryonic deaths are common and late abortion from four months gestation to term are occasionally observed. Often the presence of the disease is unsuspected until the veterinarian finds many nonpregnant females during routine pregnancy examination made in autumn. Along with nonpregnant cows, considerable differences in fetal age may be noticed.

In a herd that has never been exposed and where no immunity exists, an acute type of infertility problem develops. In this case, infertility due to endometritis results in early embryonic death and a prolonged period of time (up to 120+ days) passes before successful conception occurs. Within this time the female develops a local immunity and clearance of the organism from the uterus occurs so that conception can take place (15). Some heifers have a natural immunity or develop immunity quickly and conceive within two months. Others may conceive early but remain carriers of the organism for months, while still others remain infected for months, require many services, and may even abort after conception (15).

The subacute or chronic form of the disease shows as a vague or intermittent infertility problem in the older cows, but susceptible females added to the herd develop the more acute form (15). Older cows that have been previously infected are more refractive to reinfection due to an anamnestic response of the already primed local immune mechanism (4,12).

Abortions can occur later in pregnancy in all instances but are more prevalent in the highly susceptible herds.

PATHOGENESIS AND IMMUNE RESPONSE

Under natural conditions, bulls transmit *Campylobacter fetus* from one female to another. Before the advent of properly handled and antibiotic treated semen, the disease could be spread by means of artificial insemination (12,15). Direct female to female spread is highly unlikely, whereas bull to bull transmission can occur among groups of bulls penned together where riding behavior is active. The organism establishes itself in the prepuce of the male but does not interfere with semen quality or breeding ability (6,15).

Organisms introduced into the cervicovaginal area at estrus do not establish themselves in the uterus until the progestational phase (17). Since neutrophils are numerous in the uterus during estrus, it was proposed (10) that they play a major role in preventing colonization at this time. Later in the cycle, when fewer neutrophils are present, *C. fetus* is able to invade the uterus.

After colonization in the uterus the organism initiates a local immune response where immunoglobulins A, G and M are synthesized (23). It would appear that these agglutinins are synthesized locally since no appreciable agglutinins can be detected in the serum after infection. Once formed, these agglutinins are very significant in the control of *C. fetus*. Corbeil *et al* (9) found that IgG was the predominant agglutinin in the uterine secretions of convalescent animals where IgA was found primarily in the cervicovaginal mucus. IgG acts as an opsonin, thus aiding neutrophils and macrophages in the phagocytosis of *C. fetus*. IgA, on the other hand, only immobilizes the organism and this could explain the ability of *C. fetus* to remain in the cervicovaginal area in some convalescent animals, thus maintaining a carrier state. Under these circumstances, a cow could conceive during a later heat cycle while still carrying the organism in the cervicovaginal area (4). There is also a suggestion of cell mediated immunity involving complement later in infection when lymphocytes are numerous (17).

In systemically immunized animals only IgG is found in the uterus and cervicovaginal secretions (9), thus enabling the clearance of *C. fetus* from the uterus and cervicovaginal area, providing the serum titer of IgG is adequate at the time of exposure (4). Serum antibody titers tend to decrease rapidly after vaccination therefore a corresponding reduction in immunity is to be expected. Reinfection subsequent to vaccinal immunity fails to produce a systemic anamnestic response (4).

Hoerlein *et al* (12) found that once the disease becomes established in a herd, the resistance to infection increase, and the conception rate for the older cows returns to near normal. It was proposed that upon reinfection the organisms have immediate access to the already primed local immune mechanism (4). Thus, in contrast to vaccinal immunity, there is evidence for a local anamnestic response upon reinfection.

Spread of the organism to the male is primarily by way of copulation with an infected female although direct bull to bull spread is possible. Young bulls under five years of age are difficult to infect (16); however, some workers (6) found that both younger and older bulls could remain carriers for up to 18 weeks postinfection. Older bulls tend to retain the infection more permanently than younger bulls possibly due to the increase in number and size of the crypts in the epithelium of the penis (16). The greatest concentration of *C. fetus* is in the fornix of the prepuce and on the penis. The lumina of the epithelial crypts carry the highest concentration of *C. fetus* organisms, suggesting these as major sites of proliferation (16).

Bier *et al* (6) found that preputial fluid titers of agglutinins against *C. fetus* were low in samples obtained both before and after infection. Lack of sufficient antigenic stimulation by the organism, which is restricted to the epithelial surface (16), may explain the absence of appreciable antibody formation and may be an important factor in prolonged survival of *C. fetus* in the preputial cavity. Changes in the composition of the superficial antigen of *C. fetus* occur during infection of the preputial cavity (6). Although the mechanism underlying antigenic variation of *C. fetus* is unexplained, it is possible that low levels of preputial antibodies may have been sufficient to act in selection of antigenically altered organisms. Antigenic variation of the bacteria might be an additional factor enhancing the persistence of the carrier state in bulls as well as heifers (16).

PATHOLOGY

Endometritis, mild cervicitis and salpingitis are usually the only lesions occurring in *C. fetus* infection of the genital tract of cows and heifers (15). Grossly the cervix may be reddened and the uterus may have a slight mucopurulent exudate that can extend through the cervix into the vagina.

Histologically these changes are not striking and consist, for the most part, of a diffuse but light infiltration of inflammatory cells with slight desquamation of the superficial epithelium and no significant vascular changes (13). Endometrial glandular involvement is minimal however on resolution there may be a few cystic glands with slight periglandular fibrosis (13). The best indication of mild endometritis are infiltration of plasma cells and foci of lymphocytes in the stroma.

Gross abnormalities of the preputial or penile mucosa are not usually observed in bulls (5). Histologically there is a diffuse infiltration of mononuclear cells within the lamina propria. Plasma cells are located generally in clusters at the apex of the dermal papillae, especially in older bulls (6).

DIAGNOSIS

A definitive diagnosis of genital vibriosis can be difficult and the results of laboratory tests are often disappointing (2). Four laboratory tests — serum agglutination, cervical mucus agglutination, fluorescent antibody and culture have been used extensively in the past; however, each of these tests has a number of limitations. Advantages and disadvantages of these individual tests have often been demonstrated but the tests have never been compared in a single infected herd until 1974 (2).

Serum agglutination (SA) is not a very reliable test for campylobacteriosis since it is not a systemic disease and antibodies are rarely found in the blood stream.

The cervical mucus agglutination test (CMA) has been used extensively, but both false positive and false negative test results can occur. However, some researchers have found the test to be a convenient and accurate method for diagnosing bovine campylobacteriosis (14). Several factors must be considered in using the mucus agglutination test. It takes approximately 60 days postinfection for the mucus to become positive on test. The duration of the positive titer averages approximately seven months (14), therefore limiting diagnosis. To use this test for determining infection in individual animals, the stage of the estrus cycle and the time of exposure to the disease must be known. Estrus mucus dilutes the agglutinins so that a false negative reaction may occur. Blood from either metestral bleeding or from rough manipulation of the vagina during collection can result in a false positive test. In the field, the CMA test can be useful for herd diagnosis. Ten animals are sufficient for examination when they can be selected according to the criteria mentioned or 20 animals if no selection is possible. In order to account for false positive titers, notation should be made of any blood appearing in the samples and of samples containing copious mucus that could indicate estrus (14). In a group of samples where there are several positive reactions, therefore suggestive of the presence of titers should be considered significant. However, little significance can be attached to one or two suspect reactions in a group of otherwise negative samples (14).

Culture and fluorescent antibody (FA) measurements gave a much larger number of positive reactions during a 40 week period than did CMA and SA tests (2). However, holding samples for a length of time, as in transit from distant areas, would reduce the chances of culturing the organism. Although vaginal mucus agglutination tests (14) and immunofluorescent procedures (21) are effective and widely used techniques for diagnosis of campylobacteriosis, isolation of the causative organism remains the only unequivocal means of establishing cause of infection (22).

A convenient transport medium for isolation of *C. fetus* in the field has been developed by Clark *et al* (8), and tested thoroughly by other workers (22). Clark's medium is convenient under field conditions because shipment can be carried out under ambient temperatures within the range of 18 to 37° C and a transit time of up to 48 hours is acceptable.

Isolation of *C. fetus* from bulls for cultural and immunofluorscent technique can be fairly successful by using Clark's transport medium. A comparison of three different sampling methods for diagnosis of genital vibriosis in the bull was made by Tedesco *et al* (20).

The conjugate used in the FA test may not differentiate between *C. fetus* subspecies *fetus* and *C. fetus* subspecies *intestinalis*, and it has been suggested that false positives may result from fecal contamination (2).

Most infected heifers rid themselves of the organism within six months of sexual rest, thus a reduction of demonstrable antibodies occurs. Therefore, at pregnancy evaluation or at calving time, when the owner first becomes aware of a proplem, only a limited number of females are still infected and antibodies may have disappeared (2).

The bacteriological examination of aborted fetuses appears to be the only practical method of confirming the diagnosis later in gestation.

CONTROL AND PREVENTION

Without vaccination, control and prevention of this disease can be a difficult problem. The use of artificial insemination that is successful in dairy herds and small farm beef herds is impractical on larger ranches. Maintaining a clean, unexposed herd is possible only if virgin bulls are used and if only clean uninfected females are introduced. In western Canada, where it is desirable to calve-out during a short period in the spring, vaccination is the only sound defence.

Berg *et al* (4) recommend that breeding herd be vaccinated twice prior to the breeding season in order to achieve a high serum IgG titer. In their experiment, heifers were vaccinated 4½ months prior to breeding followed by a booster ten days prior to breeding. The single vaccination given 4½ months before breeding failed to produce a good immune status. Since serum antibody titers decrease rapidly after vaccination, one might expect a corresponding decrease in immunity with time, therefore yearly booster vaccination is a necessity (3,4).

Cure of female cattle with venereal campylobacteriosis by systemic immunization was investigated by Schurig *et al* (18). Results of their study indicated clearly that systemic immunization of heifers with killed *C. fetus* is sufficient to cure the cervicovaginal carrier state. They also found, however, that a small percentage of females were not cured of the infection. It was proposed that the elimination of infection is dependent upon how rapidly the host mounts an

immune response versus the rate and degree of antigenic alteration of the organism.

Vaccination of bulls has been reported to be effective for both prevention (1,7) and also as a cure (18) for *C. fetus* infection. Initial vaccination should consist of two injections prior to breeding time. Annual booster vaccinations close to the time of breeding will help assure a high degree of immunity during the breeding season. It has been proposed that only bulls need vaccination because of the curative effect. However, since bulls can still passively transmit the disease under conditions of intensive sexual activity (11), the conclusion is that both males and females require immunization.

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BOOK REVIEW

Veterinary Biology and Medicine of Captive Amphibians and Reptiles. Leonard C. Marcus. Published by Lea & Febiger, Philadelphia. 1981. 239 pages. Price $30.50.

This new book fills a gap in the veterinary library.

The book is divided sensibly into three sections. The first section initiates the readers to normal animals, dealing with a variety of aspects, from anatomy to locomotion of the "side winder", to systems (endocrine, nervous, etc.). This goes into enough detail to enable understanding the animal, but does not try to make experts out of us.

The second chapter is short enough and explains normal husbandry practices applicable to herpetofauna. It explains the normal, proper care due to these fascinating animals and explains rapidly the specific methods and techniques used in examination, restraint, anesthesia . . .

The last chapter is the most extensive and gives precise information on specific diseases. The parasitic diseases are given more emphasis than the infectious diseases. This is probably a consequence of our extremely limited knowledge of bacterial and other infectious diseases of herpetofauna.

Nutritional diseases receive a good deal of attention, and represent undoubtedly some of the most common problems of these newcomers into the world of pets.

This book is very interesting and will prove to be a great help to many veterinarians and other related professionals. The relatively small size of the book and the wide range of topics it covers can only point out how much remains to be learned about these cold blooded creatures.

It will be a useful guide for many people who must deal with the problems of pets, about which most people (including the owners) know next to nothing. *C. Y. R. Gardell.*